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Prolonged-release fampridine treatment improved subject-reported impact of multiple sclerosis: Item-level analysis of the MSIS-29

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ABSTRACT

Prolonged-release (PR) fampridine is approved to treat walking impairment in persons with multiple sclerosis (MS); however, treatment benefits may extend beyond walking. MOBILE was a phase 2, 24-week, double-blind, placebo-controlled exploratory study to assess the impact of 10 mg PR-fampridine twice daily versus placebo on several subject-assessed measures. This analysis evaluated the physical and psychological health outcomes of subjects with progressing or relapsing MS from individual items of the Multiple Sclerosis Impact Scale (MSIS-29). PR-fampridine treatment ($n = 68$) resulted in greater improvements from baseline in the MSIS-29 physical (PHYS) and psychological (PSYCH) impact subscales, with differences of 89% and 148% in mean score reduction from baseline ($n = 64$) at week 24 versus placebo, respectively. MSIS-29 item analysis showed that a higher percentage of PR-fampridine subjects had mean improvements in 16/20 PHYS and 6/9 PSYCH items versus placebo after 24 weeks. Post hoc analysis of the 12-item Multiple Sclerosis Walking Scale (MSWS-12) improver population (≥8-point mean improvement) demonstrated differences in mean reductions from baseline of 97% and 111% in PR-fampridine MSIS-29 PHYS and PSYCH subscales versus the overall placebo group over 24 weeks. A higher percentage of MSWS-12 improvers treated with PR-fampridine showed mean improvements in 20/20 PHYS and 8/9 PSYCH items versus placebo at 24 weeks. In conclusion, PR-fampridine resulted in physical and psychological benefits versus placebo, sustained over 24 weeks.

1. Introduction

Walking impairment is a common disability among persons with multiple sclerosis (MS) and has a negative impact on quality of life [1,2]. Walking disability can reduce independence, with lower limb function identified as the most important bodily function in a study of persons with MS [3]. Prolonged-release (PR) oral fampridine, also known as extended release (dal)fampridine in the US, is currently the only drug approved to improve walking in persons with MS [4,5]. In two pivotal phase 3 clinical studies, treatment with PR-fampridine resulted in consistent increases in walking speed versus placebo (25.2% versus 4.7%; $P < 0.001$), for study subjects assessed as responders (consistently faster Timed 25-Foot Walk [T25FW] times on treatment versus off treatment) [6]. Improvements in the self-assessed 12-item Multiple Sclerosis Walking Scale (MSWS-12) were also reported for responders, independent of treatment assignment (nominal $P < 0.001$) [7]. Subsequent open-label extension studies in responder subjects from the two pivotal phase 3 studies showed that the efficacy and safety of PR-fampridine was maintained over a mean exposure of 39.0 and 26.3 months, with improved walking speed compared with non-responders [8].

Recent studies have demonstrated that the benefits of PR-fampridine may extend beyond walking speed. Improvements in arm function, physical and cognitive fatigue, mood and quality of life were reported in PR-fampridine–treated subjects with MS, who showed improvements in walking ability through the T25FW, MSWS-12 or 2-Minute Walk Test [9,10]. The psychological benefits of PR-fampridine were

Abbreviations: EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; MSIS-29, Multiple Sclerosis Impact Scale; MSWS-12, 12-item Multiple Sclerosis Walking Scale; PHYS, physical impact subscale; PPMS, primary-progressive multiple sclerosis; PR, prolonged-release; PRMS, progressive-relapsing multiple sclerosis; PSYCH, psychological impact subscale; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary-progressive multiple sclerosis.

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also reported in the ENABLE study, a 48-week, real-world, open-label study [11]; however, there have been no data from blinded, placebo-controlled studies in a similar setting.

The phase 2, 24-week, double-blind, randomised MOBILE study expanded upon the ENABLE study and was the first placebo-controlled study to evaluate the impact of PR-fampridine treatment on mobility, balance and the subject-perceived health impact of MS, using several self-assessed measures [12]. Results from the MOBILE study included greater median improvements from baseline in the 29-item Multiple Sclerosis Impact Scale (MSIS-29) physical subscale (PHYS) versus placebo. Additionally, a higher proportion of subjects treated with PR-fampridine achieved improvements in the clinically significant MSWS-12 ≥ 8-point reduction threshold [13] versus placebo ($P = 0.0153$) [12]. Adverse events were consistent with the established safety profile of PR-fampridine [12].

This analysis of the MOBILE study evaluated the effect of PR-fampridine versus placebo on the subject-perceived physical and psychological health impact of MS based on the 29 individual items of the MSIS-29. The self-administered MSIS-29 questionnaire contains a 20-item PHYS and a nine-item psychological impact subscale (PSYCH) and shows good variability, high internal consistency, high test-retest reliability and good responsiveness to interventions [14,15]. A post hoc analysis also evaluated MSWS-12 improvers – subjects who were treated with PR-fampridine and achieved the clinically significant ≥8-point reduction threshold in MSWS-12 score.

2. Materials and methods

2.1. Study design

MOBILE was a 24-week, randomised, double-blind, exploratory, placebo-controlled phase 2 study (ClinicalTrials.gov identifier NCT01597297; EudraCT number 2012-000368-90) that enrolled subjects with MS in Europe and Canada. This study explored the effect of PR-fampridine on self-assessed walking disability and the subjective impression of well-being in order to further elucidate thresholds for clinically meaningful changes over 6 months. Study subjects were randomised to PR-fampridine 10-mg tablets ($n = 68$) or placebo ($n = 64$) twice daily. The study was conducted in compliance with the Declaration of Helsinki and regulatory requirements, with approval obtained from local ethics committees and written informed consent provided by the study subjects. The full methods and results of the MOBILE study have been published previously [12].

2.2. Subjects

The main inclusion criteria were subjects 18 to 70 years of age with a diagnosis of progressive or relapsing MS, with a disease duration of ≥3 months and an Expanded Disability Status Scale (EDSS) score of 4.0 to 7.0. Stable concomitant therapies for MS were allowed.

2.3. Study assessments

After a screening period of 14 days, the MSIS-29 PHYS and PSYCH were assessed at screening visit, day 1 and each on-treatment visit at weeks 2, 4, 8, 12, 16 and 20, with the last treatment visit at week 24 or upon early termination from the study (Fig. 1). Negative change on the MSIS-29 PHYS and PSYCH subscales indicates improvement in physical and psychological health, respectively.

2.4. Statistical methods

Mean changes from baseline in the MSIS-29 PHYS and PSYCH subscales were calculated at each study visit, where baseline was defined as the average score over day 1 and screening. Differences between the PR-fampridine and placebo groups in the mean reductions for each visit versus baseline were given as a percentage. The mean changes for each of the 20 items of the MSIS-29 PHYS and nine items of the PSYCH were calculated using all post-baseline visits up to 24 weeks. For a particular visit, MSIS-29 PHYS and PSYCH scores were calculated by totalling the individual items and transforming to a scale with a range of 0 (no impact of MS) to 100 (extreme impact of MS). The percentage of study subjects who reported any mean improvement or worsening in the MSIS-29 PHYS and PSYCH individual items by visit, or who had a mean improvement of ≥7.0 points over weeks 2 to 24 in the MSIS-29 PHYS subscale score, were also analysed.

2.4.1. MSWS-12 responder analysis

The MSWS-12 score is a subject-reported, disease-specific measure of mobility limitations due to MS over the preceding 2 weeks, where reductions in the score indicate improvement [16]. It has been demonstrated that a ≥ 8-point mean reduction in MSWS-12 score indicates a clinically meaningful subject-level improvement in walking ability [13]. Therefore, post hoc subgroup analysis was conducted to stratify PR-fampridine–treated subjects according to MSWS-12 improver (≥8-point mean reduction in MSWS-12 score) or MSWS-12 non-improver

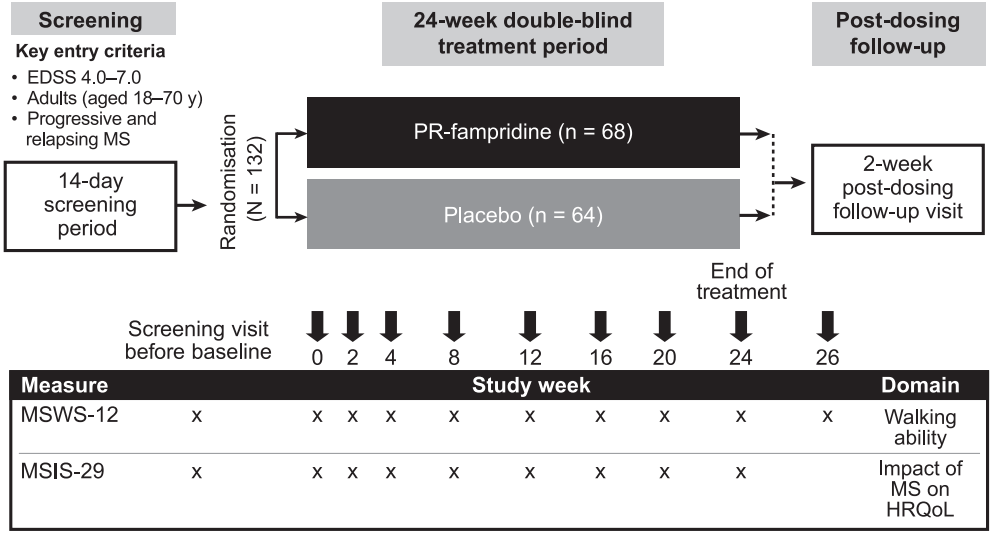

Fig. 1. Design of the MOBILE study. EDSS: Expanded Disability Status Scale; HRQoL: health-related quality of life; MS: multiple sclerosis: MSIS-29: Multiple Sclerosis Impact Scale; MSWS-12: 12-item Multiple Sclerosis Walking Score.

Table 1
Baseline characteristics.

Characteristic	Placebo ($n = 64$)	PR-fampridine ($n = 68$)
Mean (median) age, years	49.8 (50.0)	49.8 (50.0)
Male, n (%)	31 (48)	30 (44)
White, n (%)	63 (98)	66 (97)
Mean (SD) time since MS diagnosis, years[a]	12.4 (8.4)	10.9 (6.8)
Mean (SD) no. of relapses within past year[a]	0.3 (0.7)	0.2 (0.4)
Disease course, n (%)		
SPMS	37 (58)	31 (46)
RRMS	20 (31)	24 (35)
PPMS/PRMS	7 (11)	13 (19)
Mean (min–max) EDSS score	5.9 (4.0–7.0)	5.6 (4.0–7.0)
Mean (median) MSIS-29 PHYS subscale score	53.0 (57.5)	50.9 (50.0)
Mean (median) MSIS-29 PSYCH subscale score	36.3 (34.0)	36.0 (32.6)
Mean (median) MSWS-12 score	75.9 (81.3)	71.7 (75.0)

[a] Placebo, $n = 63$. EDSS: Expanded Disability Status Scale; max: maximum; min: minimum; MS: multiple sclerosis; MSIS-29: Multiple Sclerosis Impact Scale; MSWS-12: 12-item Multiple Sclerosis Walking Scale; PHYS: physical impact subscale; PPMS: primary-progressive multiple sclerosis; PR: prolonged-release; PRMS: progressive-relapsing multiple sclerosis; PSYCH: psychological impact subscale; RRMS: relapsing-remitting multiple sclerosis; SPMS: secondary-progressive multiple sclerosis.

(no change, <8 point mean reduction, or a mean increase in MSWS-12 score) status.

For MSIS-29 scores, missing data were imputed using the last observation carried forward method when at least one post-baseline value was available. Baseline values were not carried forward. Mean changes across study subjects were presented at each visit. Treatment differences were assessed using logistic regression, adjusting for mean baseline item score. For all analyses of individual items, observed data were used.

The primary objective of the MOBILE study was to provide an estimate of the effect of PR-fampridine treatment on multiple endpoints, for which a sample size of 120 study subjects was considered sufficient. However, this sample size was too small to observe significant changes in the individual item-level analysis of the MSIS-29 within the subset of subjects classified as MSWS-12 improvers. Therefore, no formal statistical testing was performed for these analyses.

3. Results

All enrolled subjects were treated and included in this analysis (placebo, $n = 64$; PR-fampridine, $n = 68$). Baseline characteristics were mostly similar between the groups (Table 1).

3.1. MSIS-29 PHYS and PSYCH subscale scores

PR-fampridine treatment resulted in greater improvements from baseline in MSIS-29 PHYS subscale scores than those for the placebo group at weeks 4, 12 and 24 (Fig. 2). The greatest mean improvements from baseline in MSIS-29 PHYS subscale scores were observed at week 4, while at week 24 there was a difference of 89% between the PR-fampridine and placebo groups in the change in MSIS-29 PHYS mean subscale score from baseline. Similar results were observed for changes in MSIS-29 PSYCH subscale scores from baseline at weeks 4, 12 and 24, with a 148% difference between the PR-fampridine and placebo groups in the mean reduction in score from baseline at week 24 (Fig. 2).

3.2. Item-level analysis of the MSIS-29 PHYS and PSYCH subscale scores

Study subjects treated with PR-fampridine also showed improved responses across most of the MSIS-29 PHYS items compared with placebo; a higher percentage of PR-fampridine subjects reported any mean reduction in 17 of the 20 individual MSIS-29 PHYS item scores over 12 weeks (Fig. 3a), and in 16 of the 20 individual items over 24 weeks (Fig. 3b). Post hoc analysis showed that these differences versus placebo were significant in three of the MSIS-29 PHYS items over 12 weeks: *difficulties moving around indoors* ($P = 0.009$), *having to cut time on work/other activities* ($P = 0.020$) and *taking longer to do things* ($P = 0.027$; Fig. 3a). Over 24 weeks, there were significant differences in the PR-fampridine group versus placebo in four of the PHYS items: *difficulties moving around indoors* ($P = 0.013$), *difficulty doing things spontaneously* ($P = 0.012$), *having to depend on others to do things* ($P = 0.017$) and *taking longer to do things* ($P = 0.040$; Fig. 3b). A higher percentage of subjects treated with PR-fampridine also showed mean improvements in six of the nine PSYCH items over 12 and 24 weeks versus placebo (Fig. 4). This difference was significantly greater for PR-fampridine versus placebo in the post hoc analysis for one item, *worries related to your MS*, over 12 weeks ($P = 0.044$; Fig. 4a) and 24 weeks ($P = 0.006$, Fig. 4b).

3.3. Post hoc analysis of the MSIS-29 PHYS and PSYCH subscale scores according to MSWS-12 response

Subjects treated with PR-fampridine demonstrated improvements in MSWS-12 score, with a median change from Baseline to the mean on-treatment period in MSWS-12 score of −6.9 (95% CI: −11.6, −1.6) points versus −2.9 (95% CI: −5.4, 1.0) points in placebo-treated subjects (median treatment difference: −3.3 [95% CI: −7.6, 1.2]). Furthermore, a strong correlation was observed between changes in MSWS-12 and MSIS-29 PHYS scores (Pearson's correlation coefficient = 0.768) and a moderate correlation between MSWS-12 and MSIS-29 PSYCH scores (Pearson's correlation coefficient = 0.483). Therefore, a post hoc subgroup analysis was conducted to provide the MSIS-29 subscale scores and item-level analysis according to MSWS-12 improver (≥8-point mean reduction in MSWS-12 score) or MSWS-12 non-improver (<8-point mean reduction, no change, or an increase in MSWS-12

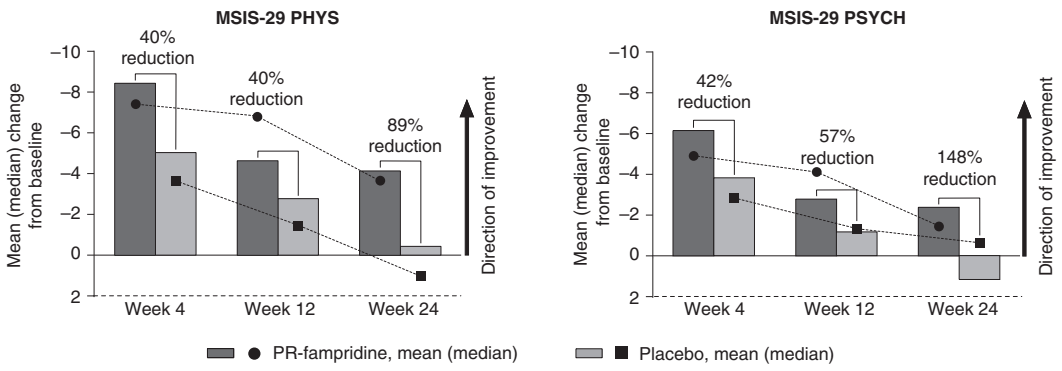

Fig. 2. Mean (median) change from baseline in Multiple Sclerosis Impact Scale (MSIS-29) physical impact (PHYS) and psychological impact (PSYCH) subscale scores at weeks 4, 12 and 24. PR: prolonged-release.

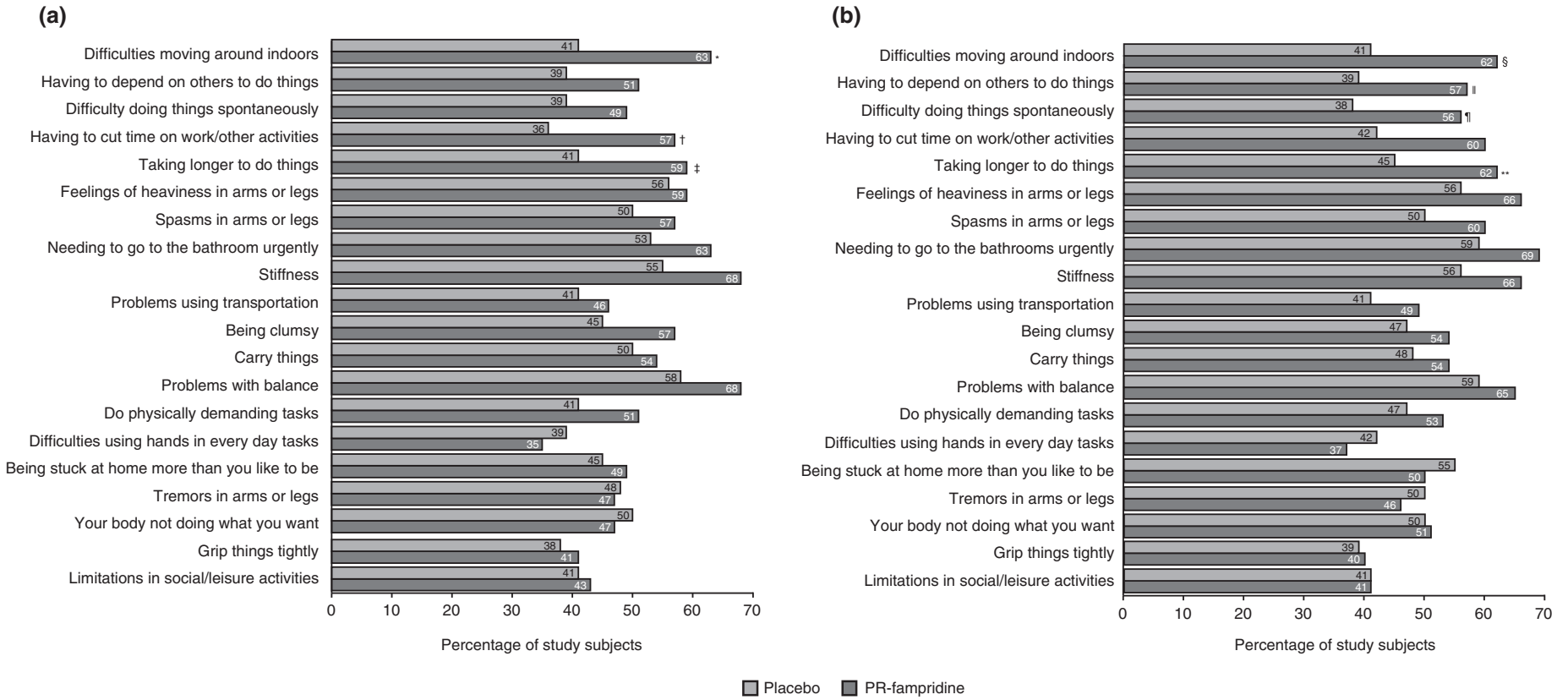

Fig. 3. Percentage of study subjects with any mean improvement in the Multiple Sclerosis Impact Scale physical impact subscale items over (a) 12 weeks and (b) 24 weeks. *$P = 0.009$; †$P = 0.020$; ‡$P = 0.027$; §$P = 0.013$; ‖$P = 0.017$; ¶$P = 0.012$; **$P = 0.040$. Items ordered by greatest treatment difference for prolonged-release (PR) fampridine versus placebo at 24 weeks.

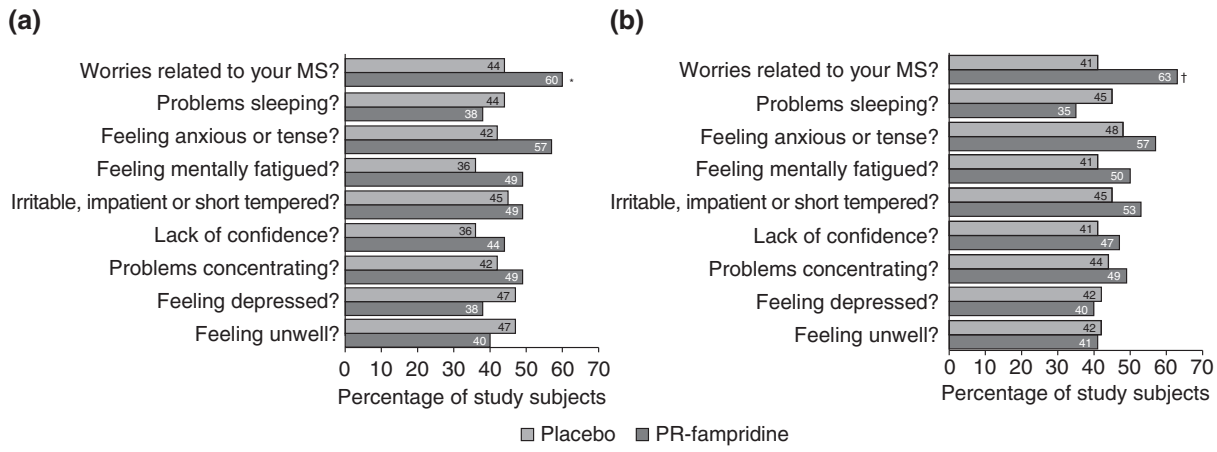

Fig. 4. Percentage of study subjects with any mean improvement in the Multiple Sclerosis Impact Scale psychological impact subscale items over (a) 12 weeks and (b) 24 weeks. *$P = 0.044$; †$P = 0.006$. Items ordered by greatest treatment difference for prolonged-release (PR) fampridine versus placebo over 24 weeks. MS: multiple sclerosis.

score) status. In the PR-fampridine group, 33 subjects were classified as MSWS-12 improvers and 35 as MSWS-12 non-improvers; in the placebo group far more subjects were classified as MSWS-12 non-improvers ($n = 46$) than MSWS-12 improvers ($n = 18$). Due the small number of placebo subjects who showed clinically meaningful improvement on the MSWS-12, analyses were conducted on the placebo group as a whole ($n = 64$).

Subjects classified as PR-fampridine MSWS-12 improvers (≥8-point mean improvement) reported an 82% difference in the mean reduction from baseline in MSIS-29 PHYS subscale scores compared with the placebo group at week 12 (Fig. 5). A higher percentage of PR-fampridine MSWS-12 improver subjects also showed any mean improvements in the MSIS-29 PHYS subscale score over 24 weeks, compared with placebo (97% difference in mean reduction).

MSWS-12 improvers also demonstrated a difference of 111% in the mean reduction in MSIS-29 PSYCH scores from baseline versus placebo ($n = 64$) at 24 weeks. Improvements from baseline observed in the PR-fampridine MSWS-12 improver population were also greater than the MSWS-12 non-improvers for both the MSIS-29 PHYS and PSYCH scores ($n = 35$).

3.4. Improvements in the MSIS-29 PHYS subscale according to MSWS-12 improver status

Thresholds for a clinically meaningful change in the MSIS-29 PHYS have been proposed to be between 7 and 8 points [17,18]. Therefore, analyses were also conducted to evaluate the percentages of subjects who achieved a ≥7-point improvement in the MSIS-29 PHYS subscale score, by MSIS-12 improver status. In the PR-fampridine MSWS-12 improver group, 82% of subjects had a mean improvement of ≥7.0 points in the MSIS-29 PHYS subscale score, versus 11% of the PR-fampridine non-improver group or 30% of the placebo group.

3.5. Item-level analysis of the MSIS-29 PHYS and PSYCH scores according to MSWS-12 improver status

When the MSIS-29 PHYS and PSYCH items were assessed according to MSWS-12 improver status for PR-fampridine–treated subjects, a higher percentage of MSWS-12 improvers reported mean reductions in 19 of the 20 MSIS-29 PHYS items over 12 weeks versus placebo and non-improvers (Fig. 6a). MSWS-12 improvers also demonstrated a

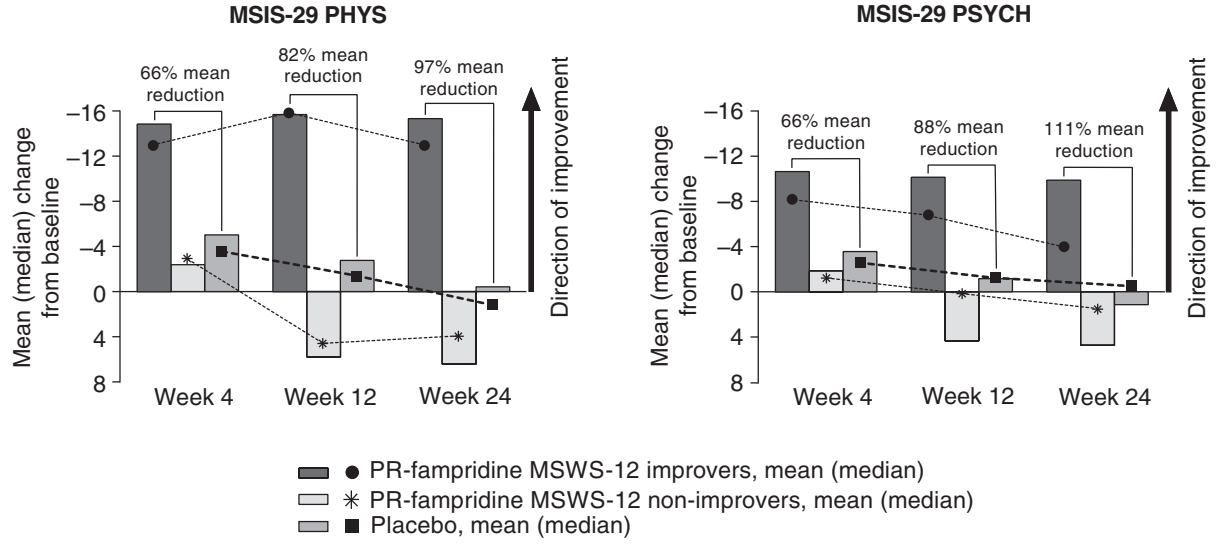

Fig. 5. Mean (median) change from baseline in Multiple Sclerosis Impact Scale (MSIS-29) physical impact subscale (PHYS) and psychological impact subscale (PSYCH) scores at weeks 4, 12 and 24 in 12-item Multiple Sclerosis Walking Scale (MSWS-12) for improver (≥8-point mean improvement), non-improver and placebo subjects.

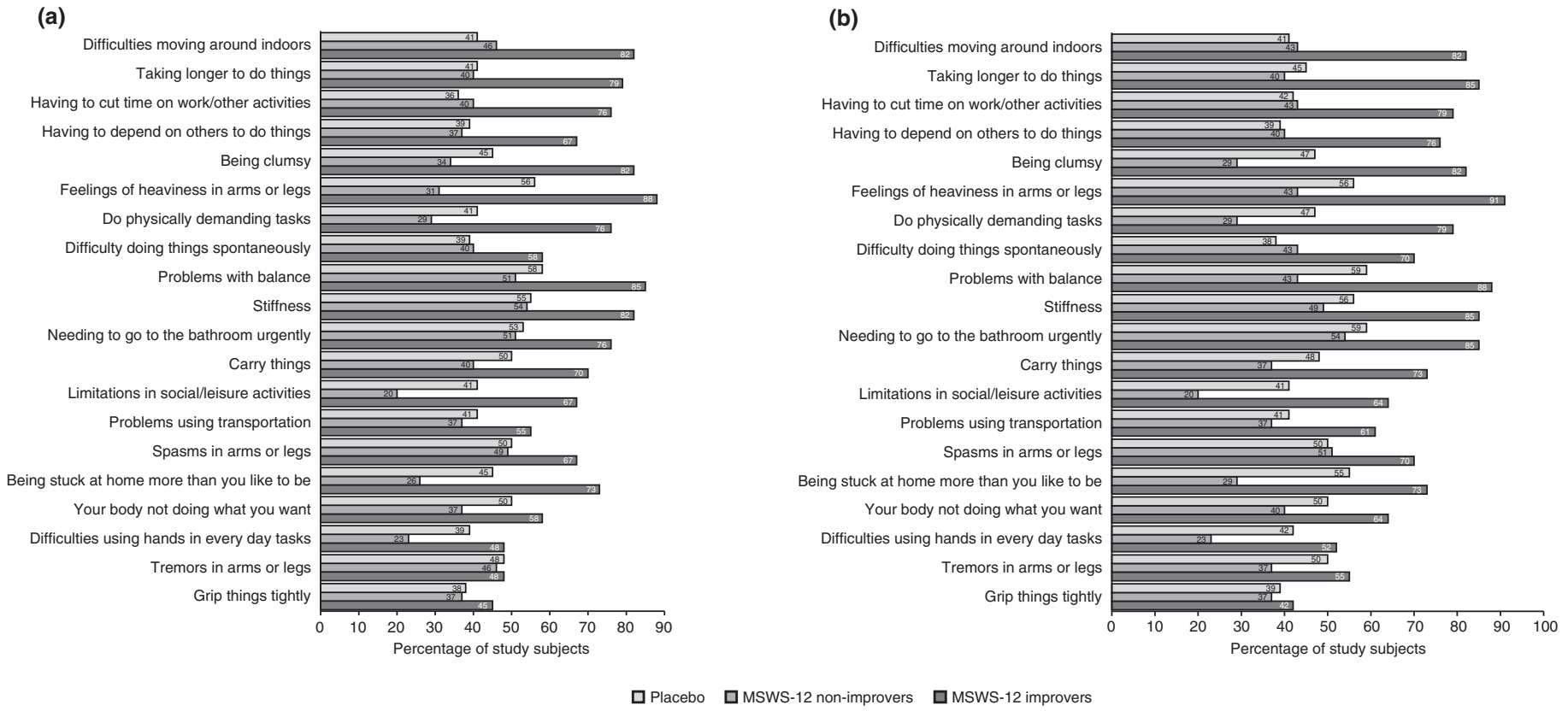

Fig. 6. Percentage of 12-item Multiple Sclerosis Walking Scale (MSWS-12) improver, non-improver and placebo subjects with any mean improvement in the Multiple Sclerosis Impact Scale physical impact subscale items from week 2 to (a) week 12 and (b) week 24. Items ordered by greatest treatment difference for MSWS-12 improvers versus placebo over 24 weeks.

higher percentage of PR-fampridine–treated subjects achieving any mean score reductions across all of the 20 PHYS items over 24 weeks compared with both the MSWS-12 non-improvers and the placebo group (Fig. 6b). Differences in the percentage of subjects achieving any improvement in individual item scores over weeks 2 to 24 were greatest (>35%) for the following four items when the MSWS-12 improver group was compared with the placebo population: *difficulties moving around indoors*, *taking longer to do things*, *having to cut time on work/other activities* and *having to depend on others to do things*.

A higher percentage of MSWS-12 improvers also achieved mean reductions in seven of the nine MSIS-29 PSYCH items compared with placebo subjects over weeks 2 to 12 (Fig. 7a), and in eight of the nine MSIS-29 PSYCH items over weeks 2 to 24 (Fig. 7b). There was a higher percentage of MSWS-12 improvers with mean reductions in scores across all MSIS-29 PSYCH items over weeks 2 to 12 and also weeks 2 to 24 compared with MSWS-12 non-improvers. The two items with the greatest percentage difference (>25%) in study subjects demonstrating any mean reductions in the MSWS-12 improver group versus placebo subjects over weeks 2 to 24 were *feeling mentally fatigued* and *worries related to your MS*.

4. Discussion

MS is a debilitating disease that can result in walking impairment [1,19]. Previous studies have demonstrated an association between walking speed and quality of life, suggesting that greater walking disability leads to reduced quality of life [2]. In the pivotal phase 3 clinical studies, PR-fampridine was shown to improve walking ability [6,7], while post-marketing and placebo-controlled studies also demonstrated improvements in dynamic and static balance [12,20].

In MOBILE, PR-fampridine showed benefits in subjects with MS on subject-assessed walking ability assessed using the MSWS-12, including numerically larger median improvements compared with placebo [12]. In addition to these benefits, results from the current analyses of the MOBILE study indicate that PR-fampridine treatment improved the self-assessed physical and psychological health impact of MS. PR-fampridine treatment resulted in mean reductions in the MSIS-29 PHYS and PSYCH subscale scores, with a higher percentage of study subjects showing improvements across the majority of the PHYS and PSYCH items versus placebo. Evaluation of the MSWS-12 improvers demonstrated that the physical and psychological benefits of PR-fampridine were improved to a greater extent in those who showed a clinically meaningful increase in walking speed.

Thresholds for clinically meaningful worsening in the MSIS-29 PHYS subscale score have been established in both the clinical trial and the community setting [17,18]. Clinically meaningful worsening in the MSIS-29 PHYS subscale score was reported as ≥7.5 points in a clinical trial population [17] and ≥7.0 points in a community setting [18], for subjects with MS and an EDSS score of 0 to 5 [17]. For subjects based in a community setting with an EDSS score of 5.5 to 8, the clinically meaningful threshold for MSIS-29 PHYS subscale worsening was reported as ≥8 points [18]. A threshold for *improvement* in the MSIS-29 PHYS subscale score has yet to be established, to the authors' knowledge. However, a ≥7-point change in MSIS-29 PHYS subscale score provides a good estimate of subjects who may be experiencing clinically meaningful improvements in the MSIS-29 PHYS subscale. The current analysis showed that the majority of the PR-fampridine–treated MSWS-12 improver subjects (82%) also showed ≥7-point mean improvement in the MSIS-29 PHYS subscale score over weeks 2 to 24 of treatment. Few subjects (11%, $n = 4$) in the PR-fampridine MSWS-12 non-improver group met this threshold for improvement in the MSIS-29 PHYS subscale score. These post hoc results provide additional support that improvements in walking ability are consistent with better subject-reported physical functioning.

Progression of the MSIS-29 PHYS and PSYCH subscale scores for the PR-fampridine population were similar throughout the study, consistent with findings from the open-label, 48-week ENABLE study [11]. Improvements observed across both the MSIS-29 PHYS and PSYCH subscale scores for PR-fampridine–treated subjects in this analysis are consistent with those reported by Hoogervorst et al., who described good correlation between PHYS and PSYCH subscale scores ($r = 0.62$) in a large, independent population of persons with MS [21]. A Swedish registry study of natalizumab also showed improvements across both the PHYS and PSYCH subscale scores after 24 months, indicating that physical health improvements are linked to definable psychological benefits in persons with MS [22]. It should be noted that the results assessing psychological impact in this analysis showed greater variability compared with the physical impact.

Results show that treatment with PR-fampridine improved the subject-perceived physical health impact of MS, extending findings from the open-label ENABLE study, which demonstrated significant improvements in the mean MSIS-29 PHYS subscale change from baseline versus placebo at weeks 12 and 24. Significant improvements in MSIS-29 PHYS subscale score were subsequently maintained throughout the 48 weeks of the ENABLE study [11].

Consistent with the improvement in overall MSIS-29 PHYS subscale score, higher percentages of PR-fampridine–treated subjects demonstrated reductions in scores across 16 of the 20 individual MSIS-29 PHYS items versus placebo over 24 weeks, with differences being statistically significant for four items. When study subjects were analysed according to whether they achieved a clinically significant improvement on the MSWS-12 (≥8-point mean reduction), greater percentages of MSWS-12 improvers reported reductions across all of the 20 MSIS-29 PHYS items versus both the placebo and MSWS-12 non-improver populations over weeks 2 to 24. As a higher percentage of the MSWS-12 improver group reported improvements across items such as *having to depend on others to do things*, *taking longer to do things* and *having to cut time on work/other activities*, the greater independence gained through improved walking ability in these subjects may lead to a more active life and improved overall physical outcomes. The results of the MSIS-29 PHYS item-level analysis of the PR-fampridine–treated MSWS-12 improver subjects provide further insight into the impact of improved walking ability on the health-related quality of life of persons with MS.

The psychological benefits of PR-fampridine treatment reported here are also consistent with previous reports, with the ENABLE study demonstrating significant improvements ($P < 0.001$) in the MSIS-29 PSYCH and 36-Item Short Form Health Survey mental component summary scores at weeks 12 and 24 versus subjects who did not receive treatment [11]. As reported in previous studies, improvements in walking ability, arm function, fatigue, mood and quality of life following PR-fampridine treatment may contribute to the psychological benefits observed here [9,10]. Further evaluation of the benefits observed with PR-fampridine in the MSIS-29 PSYCH item-level analysis demonstrated improvements across six of the nine PSYCH items compared with placebo over 24 weeks. It is worth noting that a higher percentage of PR-fampridine–treated and MSWS-12 improver subjects reported mean improvements for the MSIS-29 PSYCH item *feeling mentally fatigued* versus placebo, consistent with findings from Allart et al., who reported significant and prolonged improvements in fatigue after 3 months of treatment with PR-fampridine [9]. Interestingly, both MSWS-12 improver and non-improver study subjects reported greater mean improvements in *worries related to your MS* compared with placebo.

The MOBILE study showed that PR-fampridine treatment was associated with consistent subject-reported improvements in the physical and psychological measures of MS versus placebo. Analysis of the MSWS-12 improver population indicated that subjects who experience clinically meaningful improvements in walking ability show greater physical and psychological quality of life benefits.

Limitations of this study include a small sample size, the exploratory nature of the study and that some of the analyses were performed post hoc. Evaluation of the study subjects following completion of the wash-

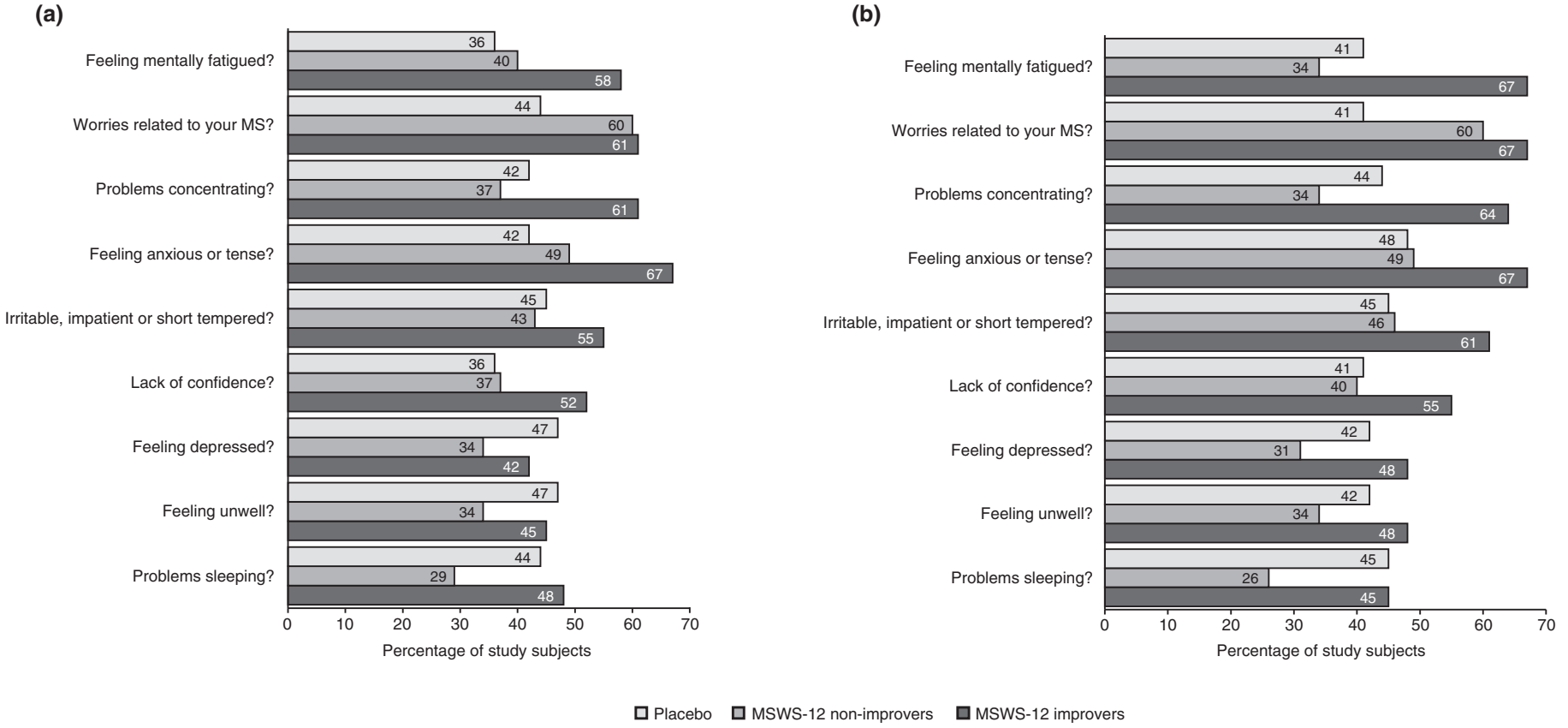

Fig. 7. Percentage of 12-item Multiple Sclerosis Walking Scale (MSWS-12) improver, non-improver and placebo subjects with any mean improvement in Multiple Sclerosis Impact Scale psychological impact subscale items from week 2 to (a) week 12 and (b) week 24. Items ordered by greatest treatment difference for MSWS-12 improvers versus placebo over 24 weeks. MS: multiple sclerosis.

out period could have further clarified whether the physical and psychological benefits versus placebo were attributable to PR-fampridine. The findings from this study need to be confirmed in a larger placebo-controlled study, which is currently underway.

5. Conclusions

The results of the MOBILE study suggest that the benefits of PR-fampridine extend beyond walking speed and also improve the subject-perceived physical and psychological impact of MS versus placebo, particularly in those who show clinically meaningful increases in walking ability.

Conflict of interest

Dr Gasperini has received consulting fees from Bayer HealthCare and Biogen; speaker fees from Bayer HealthCare, Biogen, Genzyme, Merck Serono, Novartis and Teva. Dr Hupperts has received compensation for consulting, advisory boards and research grants and as a speaker for lectures from Biogen, Genzyme, Merck, Novartis and Teva. Dr Lycke has received compensation for consulting, serving on scientific advisory boards and as a speaker for lectures from Biogen, Genzyme, Novartis and Teva. Dr Short has received compensation for serving on scientific advisory boards and as a speaker for lectures from Biogen. M. McNeill and Dr Zhong are full-time employees of and hold stock/stock options in Biogen. Dr Mehta was an employee of Biogen at the time of this study and holds stock/stock options in Biogen; Dr Mehta is currently an employee of Amgen.

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